AMENDMENTS TO THE CLAIMS

1. (Currently amended) A method to aid in predicting susceptibility of a mammalian subject to development or growth of a steroid hormone responsive cancer in a mucosal epithelial tissue, the method comprising:

quantitating and/or detecting ~~a steroid hormone reversible~~an immunoglobulin inhibitor of steroid hormone responsive cell growth in a body fluid or secretion obtained from said subject, wherein said inhibition of steroid hormone responsive cell growth is capable of being reversed by binding a steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth,

an absence or deficiency of said immunoglobulin inhibitor ~~compared to a predetermined standard~~ suggesting or indicating that a steroid hormone responsive mucosal epithelial tissue in said subject secretes or is bathed by less than a ~~predetermined~~ cell growth inhibitory amount of said immunoglobulin inhibitor.

2. (Original) The method of claim 1 further comprising obtaining a sample of body fluid or secretion chosen from the group consisting of serum, plasma, colostrum, breast aspirates, saliva, tears, bronchial secretions, nasal mucosa, prostatic fluid, urine, semen or seminal fluid, vaginal secretions, ovarian aspirates, stool, and mucous secretions from the small intestine or stomach.

B1°

3. (Currently amended) The method of claim 1 wherein said quantitating and/or detecting comprises measuring the amount and/or activity of ~~an~~ said immunoglobulin inhibitor in a specimen ~~comprising a defined amount~~ of body fluid or secretion from said subject.

4. (Currently amended) The method of claim 1 wherein said quantitating and/or detecting comprises substantially depleting steroid hormone from said ~~specimen~~ body fluid or secretion to yield a steroid hormone depleted specimen, and assaying ~~an aliquot of~~ said steroid hormone depleted specimen for steroid hormone reversible inhibition of steroid hormone responsive cancer cell proliferation.

5. (Currently amended) The method of claim 4 wherein said assaying comprises:

maintaining a ~~predetermined~~ population of steroid hormone-responsive cancer cells in a nutrient medium containing calcium ion and substantially no free ferric ion, said cells also being steroid hormone responsive for *in vivo* proliferation if implanted in a suitable host;

adding ~~a predetermined amount of said~~ steroid hormone to said medium~~, said amount being~~ sufficient to stimulate cell growth under cell growth promoting culture conditions;

adding ~~a predetermined an amount of~~ a steroid hormone free specimen of a body fluid or secretion to said medium, to yield a test mixture;

incubating said test mixture ~~for a predetermined period of time~~ under cell growth promoting conditions;

after said incubating, measuring the cell population in said test mixture ~~after said predetermined period of time~~;

measuring the cell population in a control incubation mixture like said test mixture, except lacking ~~an amount of~~ said specimen;

optionally, testing said ~~amount of~~ specimen for cytotoxic effects on said cells;

measuring the differences in cell number between said cell populations before and after said incubation ~~period~~, a significant increase in said cell population indicating the absence of inhibition of cell growth by said ~~amount of~~ specimen in the presence of said ~~predetermined amount of~~ steroid hormone, and a significant lack of increase in said cell population not attributable to cytotoxic effects of said ~~amount of~~ specimen indicating inhibition of cell growth by said ~~amount of~~ specimen in the presence of said ~~predetermined amount of~~ steroid hormone.

6. (Currently amended) The method of claim 5 wherein said adding of steroid hormone to said medium comprises adding an ~~predetermined~~ amount of steroid hormone that is in the physiological concentration range for said steroid hormone in said mammal.

7. (Currently amended) An *in vitro* method of detecting loss of immunoglobulin regulation of steroid hormone responsive cell growth comprising:

determining that a poly-Ig receptor in a non-cancerous mucosal epithelial cell has the property of being able to mediate inhibition by IgA or IgM of steroid hormone responsive cell growth, wherein said inhibition of steroid hormone responsive cell growth is reversible by binding said steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth; and

assaying for inability of a mucosal epithelial cell to bind ~~at least one immunoglobulin chosen from the group consisting of~~ IgA, or IgM ~~and IgG1~~ by other than antibody-antigen recognition based association.

8. (Currently amended) A method of detecting a mediator of immunoglobulin inhibition of steroid hormone responsive cell growth wherein said inhibition can be reversed by binding a steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth, the method comprising:

detecting a poly-Ig receptor ~~or an Fcγ receptor~~ in a mucosal epithelial cell;;

optionally, testing said poly-Ig receptor for *in vitro* activity for~~being capable of~~ mediating said steroid hormone reversible immunoglobulin inhibition of steroid hormone responsive cell growth ~~in a suitable *in vitro* cell culture assay;~~

determining that said poly-Ig receptor is capable of mediating immunoglobulin inhibition of steroid hormone responsive cell growth wherein said inhibition is capable of being reversed by binding steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth.

9. (Currently amended) A method of detecting a gene coding for a mediator of immunoglobulin inhibition of steroid hormone responsive cell growth comprising:

detecting the presence of a poly-Ig receptor gene ~~or a Fcγ receptor gene~~ in a mucosal epithelial cell; and

determining whether a poly-Ig receptor encoded by said gene has the property of being capable of mediating steroid hormone reversible immunoglobulin inhibition of steroid hormone responsive cell growth wherein said inhibition is reversed by binding a steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth.

10. (Currently amended) A method of detecting a genetic defect in a gene coding for a mediator of immunoglobulin inhibition of steroid hormone responsive cell growth comprising:

identifying a loss of heterozygosity or an allelic imbalance in a poly-Ig receptor gene; or

carrying out site directed mutagenesis in a non-cancer tissue culture cell model whereby a domain of a poly-Ig receptor gene is altered,

identifying at least one said altered domain in said poly-Ig receptor gene that causes loss of ability of said poly-Ig receptor to mediate inhibition of steroid hormone responsive cell growth by an immunoglobulin inhibitor, wherein said inhibition is capable of being reversed by binding a steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth;

screening a genomic or cDNA library of a cancerous mucosal epithelial cell for a poly-Ig receptor gene ~~or a Fcγ receptor gene~~;

matching said screened poly-Ig receptor gene from said cancerous cell to a poly-Ig receptor gene from said non-cancerous cell culture model which contains an altered domain that is correlated to loss of inhibition mediating ability, whereby a genetically defective poly-Ig receptor gene is identified.

11. (Currently amended) A method of detecting expression of a defective mediator of immunoglobulin inhibition of steroid hormone responsive cell growth in a specimen of mucosal epithelial tissue, the method comprising:

detecting a ~~defective~~ poly-Ig receptor protein ~~or a Fcγ receptor~~ in said specimen which is encoded by the genetically defective poly-Ig receptor gene identified according to the method of claim 10.

12. (Currently amended) A method to aid in predicting susceptibility of a mammalian subject to development of breast cancer comprising detecting the loss or impairment of negative regulation of breast tissue proliferation by the secretory immune system in said subject, said detecting comprising testing for loss or reduction of ~~steroid hormone reversible~~ immunoglobulin inhibition of steroid hormone responsive cell growth in said tissue, wherein said inhibition is capable of being reversed by binding a steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth.

13. (Currently amended) A method to aid in predicting increased susceptibility of a mammalian subject to development or growth of a steroid hormone responsive cancer in a mucosal epithelial tissue, the method comprising:

assaying a specimen of mucosal epithelial tissue obtained from said subject for the presence of a poly-Ig receptor; and

optionally, determining whether said poly-Ig receptor is capable of mediating ~~steroid hormone reversible~~ immunoglobulin inhibition of steroid hormone responsive cell growth ~~in a suitable *in vitro* cell culture assay~~, wherein said inhibition is capable of being reversed by binding a steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth,

an absence of said receptor or an absence of activity of said receptor for mediating said immunoglobulin inhibition suggesting that said tissue lacks sufficient functional mediators of immunoglobulin inhibition to deter development or growth of a steroid hormone responsive cancer in said mucosal epithelial tissue.

14. (Currently amended) A method to aid in detecting transformation of a mucosal epithelial cell from normally steroid hormone responsive to a steroid hormone responsive cancerous condition, the method comprising:

determining that a Fcγ receptor has the property of being able to mediate inhibition by IgG1 or IgG2 of steroid hormone responsive cell growth, wherein said inhibition is capable of being reversed by binding a steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth;

optionally, testing said cells for presence of a Fcγ receptor; and

assaying a population of said mucosal epithelial cells for loss of said receptor or inactivity of ~~a~~ said receptor for binding~~that mediates~~ IgG1 or IgG2 ~~inhibition of cell growth~~, wherein inactivity for binding IgG1 or IgG2 is suggestive of said transformation.

15. (Currently amended) A method to aid in detecting progression of a steroid hormone responsive malignant mucosal epithelial cell to an autonomous cancer cell, the method comprising:

determining that a poly-Ig receptor has the property of being able to mediate inhibition by IgA or IgM of steroid hormone responsive cell growth, wherein said inhibition is capable of being reversed by binding a steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth;

optionally, testing said cells for presence of a poly-Ig receptor;

testing said autonomous cancer cell for ~~loss or inactivity of a receptor that mediates~~ ability to bind IgA ~~and/~~or IgM by other than antibody-antigen recognition based association ~~inhibition of steroid hormone responsive cancer cell growth~~.

16. (Cancelled)

17. (Currently amended) A method to aid in detecting or diagnosing cancer in a mammalian subject comprising determining, in a population of cells taken from a mucosal epithelial tissue specimen obtained from said subject, at least one of a first set of conditions selected from the following:

absence or diminution of immunoglobulin inhibition of steroid hormone responsive cell growth, wherein said inhibition is capable of being reversed by binding a steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth;

absence or diminution of at least one immunoglobulin inhibitor of steroid hormone responsive cell growth from a body fluid or secretion secreted by or bathing said tissue, wherein inhibition by said inhibitor is capable of being reversed by binding a steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth.

absence or diminution of a poly-Ig receptor in said cells,

absence of a poly-Ig receptor gene from said cells,

absence of heterozygosity for said poly-Ig receptor gene in said cells,

absence or diminution of a Fcγ receptor in said cells,

absence of a Fcγ receptor gene from said cells,

absence of heterozygosity for said Fcγ receptor gene in said cells,

and, optionally, detecting at least one of a second set of conditions selected from the following:

absence or diminution of TGFβ regulation of cell growth,

absence or diminution of a TGFβ receptor in said cells,

absence of a TGFβ receptor gene from said cells,

absence of heterozygosity for said TGFβ receptor gene in said cells,

said absence or diminution ~~being measured by comparison to similar determinations in non-neoplastic cells from said patient and/or to the patient's previous test results, or by comparison to a predetermined standard value, the presence of at least one said condition~~ being suggestive or indicative of the presence of a cancerous or precancerous lesion in said patient, and an absence of one or more of said conditions being suggestive or indicative of the absence of a cancerous or precancerous lesion in said patient.

18. (Currently amended) A method to aid in staging a cancer of a mucosal epithelial tissue comprising:

determining, in a specimen of neoplastic cells obtained from said cancer, ~~if~~ whether said cells are stimulated by a steroid hormone to proliferate in a suitable cell growth nutrient medium;

if it is determined that said cells are ~~capable of being~~ stimulated by ~~a~~ said steroid hormone to proliferate, determining the amount of immunoglobulin inhibitor in a specimen of body fluid or secretion secreted by or bathing said mucosal epithelial tissue, wherein inhibition by said immunoglobulin inhibitor is capable of being reversed by binding a steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth; ~~and~~

determining at least one of the following conditions:

loss or diminution of a TGFβ receptor in said cells,

loss of a TGFβ receptor gene in said cells ~~in said cells~~,

loss of heterozygosity for said TGFβ receptor gene in said cells,

loss or diminution of a poly-Ig receptor in said cells,

loss of a poly-Ig receptor gene in said cells,

loss of heterozygosity for said poly-Ig receptor gene in said cells,

loss or diminution of a Fcγ receptor in said cells,

loss of a Fcγ receptor gene in said cells,

loss of heterozygosity for said Fcγ receptor gene in said cells.

19. (Currently amended) A method to aid in prognosis of a mammalian cancer patient comprising:

obtaining from said patient a specimen of body fluid, a secretion secreted by or bathing a mucosal epithelial tissue, or neoplastic cells from a mucosal epithelial tissue;

~~determining at least one of the following conditions:~~

in ~~a~~ said specimen of body fluid or secretion ~~secreted by or bathing a mucosal epithelial tissue obtained from said patient~~, determining the lack of a cell growth inhibitory amount of at least one immunoglobulin inhibitor of steroid hormone responsive cell growth, wherein inhibition by said immunoglobulin inhibitor is capable of being reversed by binding a steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth, and

determining at least one of the following conditions:

in ~~a~~ said specimen of neoplastic cells from said tissue, the loss or diminution of a TGFβ receptor,

in ~~a~~ said specimen of neoplastic cells from said tissue, the loss of a TGFβ receptor gene,

in ~~a~~ said specimen of neoplastic cells from said tissue, the loss of heterozygosity for said TGFβ receptor gene,

in ~~a~~ said specimen of neoplastic cells from said tissue, the loss or diminution of a poly-Ig receptor,

in ~~a~~ said specimen of neoplastic cells from said tissue, the loss of a poly-Ig receptor gene,

in ~~a~~ said specimen of neoplastic cells from said tissue, the loss of heterozygosity for said poly-Ig receptor gene,

in ~~a~~ said specimen of neoplastic cells from said tissue, the loss or diminution of a Fcγ receptor,

in ~~a~~ said specimen of neoplastic cells from said tissue, loss of a Fcγ receptor gene,

in ~~a~~ said specimen of neoplastic cells from said tissue, loss of heterozygosity for said Fcγ receptor gene,

~~said loss or diminution being determined by comparison to similar determinations in non neoplastic cells from said patient or by comparison to defined standard values~~, the presence of one or more of said conditions being suggestive or indicative of at least some degree of reduced prognosis of said patient, and an absence of one or more of said conditions being suggestive or indicative of at least some degree of favorable prognosis.

20. (Original) A method to aid in treating cancer of a mucosal/epithelial tissue comprising detecting in a population of cancer cells obtained from said tissue the presence of ERγ.

21. - 65. (Cancelled)

66. (New) The method of claim 5 wherein said significant increase or significant lack of increase in said cell population is determined using the student's *t* test and wherein a value of $p < 0.05$ is significant.

67. (New) The method of claim 8 comprising testing said poly-Ig receptor for activity for mediating steroid hormone reversible inhibition by IgA or IgM of steroid hormone responsive cell growth.

68. (New) A method of detecting a mediator of immunoglobulin inhibition of steroid hormone responsive cell growth wherein said inhibition can be reversed by binding a steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth, the method comprising:

detecting an Fcγ receptor in a mucosal epithelial cell;

optionally, testing said Fcγ receptor for *in vitro* activity for mediating said steroid hormone reversible immunoglobulin inhibition of steroid hormone responsive cell growth;

determining that said Fcγ receptor is capable of mediating ~~steroid hormone reversible~~ immunoglobulin inhibition of steroid hormone responsive cell growth wherein said inhibition is capable of being reversed by binding a steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth.

69. (New) A method of detecting expression of a defective mediator of immunoglobulin inhibition of steroid hormone responsive cell growth in a specimen of mucosal epithelial tissue, the method comprising:

detecting a Fcγ receptor protein in said specimen which is encoded by the genetically defective Fcγ receptor gene identified according to the method of claim 80.

70. (New) The method of claim 1 wherein said immunoglobulin inhibitor comprises IgA, IgM, IgG1 or IgG2.

71. (New) An *in vitro* method of detecting loss of immunoglobulin regulation of steroid hormone responsive cell growth comprising:

determining that an Fcγ receptor in a non-cancerous mucosal epithelial cell has the property of being able to mediate immunoglobulin inhibition of steroid hormone responsive cell growth, wherein said inhibition of steroid hormone responsive cell growth is capable of being reversed by binding said steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth; and

assaying for inability of a mucosal epithelial cell to bind IgG1 or IgG2 by other than antibody-antigen recognition based association.

72. (New) A method of detecting a gene coding for a mediator of immunoglobulin inhibition of steroid hormone responsive cell growth comprising;

detecting the presence of a Fcγ receptor gene in a mucosal epithelial cell; and

determining whether a Fcγ receptor encoded by said gene has the property of being capable of mediating immunoglobulin inhibition of steroid hormone responsive cell growth, wherein said inhibition is reversible by binding a steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth.

B 10

73. (New) The method of claim 1 further comprising detecting a poly-Ig receptor in said mucosal epithelial cell.

74. (New) The method of claim 1 further comprising detecting a Fcγ receptor in said mucosal epithelial cell.

75. (New) The method of claim 74 further comprising assessing the activity of said Fcγ receptor for mediating inhibition by IgG1 or IgG2 of steroid hormone responsive cell growth in a suitable *in vitro* cell culture assay, wherein said inhibition is capable of being reversed by binding a steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth.

76. (New) The method of claim 1 comprising identifying an age range in said mammalian subject of increased susceptibility to developing breast cancer after exposure to a carcinogen.

77. (New) The method of claim 20 comprising increasing the number of B immunocytes in said mucosal/epithelial tissue producing IgA or IgM.

78. (New) The method of claim 20 comprising identifying an antagonist of ERγ.

79. (New) The method of claim 78 wherein said antagonist comprises tamoxifen.

80. (New) A method of detecting a genetic defect in a gene coding for a mediator of immunoglobulin inhibition of steroid hormone responsive cell growth comprising:

identifying a loss of heterozygosity or an allelic imbalance in a Fcγ receptor gene; or

carrying out site directed mutagenesis in a non-cancer tissue culture cell model whereby a domain of a Fcγ receptor gene is altered,

identifying at least one said altered domain in said poly-Ig receptor gene that causes loss of ability of said Fcγ receptor to mediate inhibition of steroid hormone responsive cell growth by an immunoglobulin inhibitor, wherein said inhibition is capable of being reversed by binding a steroid hormone to a cellular steroid hormone receptor that is active for promoting cell growth;

screening a genomic or cDNA library of a cancerous mucosal epithelial cell for a Fcγ receptor gene;

matching said screened Fcγ receptor gene from said cancerous cell to a Fcγ receptor gene from said non-cancerous cell culture model which contains an altered domain that is correlated to loss of inhibition mediating ability, whereby a genetically defective Fcγ receptor gene is identified.